

# Roscoe B. Jackson Memorial Laboratory

BAR HARBOR, MAINE

June 4, 1956

Cable Address  
"JAXLAB"

Dr. Joshua Lederberg  
Department of Genetics  
University of Wisconsin  
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Madison 6, Wisconsin

Dear Dr. Lederberg:

Thanks very much for the reprints which I am much pleased indeed to receive.

Over the past four or five years Nate and I have dreamed up ourselves or had suggested to us an extraordinary variety of hypothesis to account for the enhancing effect. Recent experiments have narrowed these down very considerably and we now begin to get a real picture of the basis of the phenomenon. It is probably a rather specialized situation. One of ~~many~~<sup>my</sup> original ideas concerning it, suggested by a knowledge of Ray Owen's work, but before Medawar's demonstration of tolerance induced by treatment of the embryo, was that it might be a tolerance phenomenon in what is now the accepted sense of this word. This explanation now appears to be ruled out however. Evidently, contrary to the first guess of both Medawar and myself, there are several types of immune blockage or tolerance. In the forthcoming issue of Transplantation Bulletin there are notes by both Billingham, Brent and Medawar and myself in which we arrive at similar conclusions about the enhancing effect. As Nate Kaliss has shown an antibody is essential to the phenomenon. It is surprising to find a reversal of immunity due to an antibody although apparently the professional immunologist accepts this a little more readily than a novice in this field such as I am. The exact way in which the antibody works is still a matter of speculation but the guess which both Medawar and I have advanced is that it in some way blocks the passage of antigens from the tumor to the regional lymph nodes thus preventing the development of the cellular immunity which is most potent in blocking the growth of homografts.

Whether tolerance in the sense in which Medawar uses this term can be induced in the adult is still an open question. There is some evidence that it can.

If I remember correctly you recently suggested that the isogenic resistant lines of mice could be used for a study of mutations in tumor by working with tumors of the F<sub>1</sub> hybrid. I have just got a letter from Avrion Mitchison in which he describes exactly this experiment. The results promised to be of great interest; he seems to get sharp transformation to tumor types that will grow in the parental types. He speculates that this may be due to ~~systemic~~<sup>somatic</sup> crossing over. It looks as if he were going to have something very fascinating here. *Avrion, I see on re-reading his letter, mentions some papers in Ann. N.Y. Acad. Sci.*

With regards and best wishes, I am

Sincerely yours,

*G. D. Snell*  
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